

# No false negative paradox in STEMI-NSTEMI diagnosis

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## INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) diagnosis is based on a clinical presentation and ST-segment elevation (STE) in at least two consecutive leads. Despite being deeply rooted in both the literature and in current medical knowledge and having been pivotal in advancing reperfusion therapy for patients with acute myocardial infarction (MI), the diagnosis of STEMI presents a significant issue: What we, the authors, call the 'no false negative paradox'. This paradox potentially makes it challenging to recognise a false negative diagnosis of STEMI and makes it difficult to appreciate the significance of an acute coronary occlusion (ACO) that could benefit from early reperfusion in door-to-needle or door-to-balloon times despite the absence of STE.<sup>1</sup>

This paradox stems from the incorporation bias and feedback sanction bias detailed in subsequent paragraphs. This is an opinion paper where the patient and the public were not involved.

## THE INCORPORATION BIAS

In conducting diagnostic test accuracy studies, the selection of the population, index test and reference test prior to study execution is fundamental. However, a methodological problem arises when the index test and the reference test are identical or when they overlap which is known as 'incorporation bias'.<sup>2</sup> This bias falsely inflates the accuracy of the results of the study above their true value. During ACO, for someone to be considered 'diseased' (STEMI), the presence of parts of the

definition of 'diseased' (STE) is mandatory. This makes 'diseased' and 'positive' almost the same causing sensitivity (the ability of a test to detect true positives among the diseased) to appear as 100% because the test is essentially comparing itself to a mirror. The problem is that a perfectly sensitive test has no false negatives. Because STE is part of both the test and the disease definition, the absence of STE can be misinterpreted as the definitive absence of the disease. This issue is compounded in MI where a distinct disease with a different treatment protocol (non-STEMI (NSTEMI)) is named based on the absence of the positive test (STE).

If we consider that the pathophysiology of the disease currently called 'STEMI' is MI due to ACO, the reference test should incorporate angiographic evidence of ACO or the identification of a culprit lesion responsible for the anginal episode and MI even if spontaneous recanalisation has occurred by the time of the angiography. Incorporation bias permeates the entirety of the literature related to the STEMI paradigm. This occurs from therapeutic studies where false negatives are included and analysed in the NSTEMI group to diagnostic accuracy studies. When the outcome measure is ACO and not an overlapping definition containing STE, as defined above, a meta-analysis of STEMI criteria found a sensitivity of only 43.6%—more than half of patients with the disease do not exhibit the test that named the disease.<sup>3</sup>

## THE FEEDBACK SANCTION BIAS

Incorporation bias is a research bias. But that is not all. The cognitive processes of healthcare professionals are also compromised. By strictly defining the disease according to clinical presentation plus STEMI criteria, any patient presenting with the pathophysiological process (ACO) but without STE, whose occlusion is not emergently intervened on as it should be, will probably not be classified as a 'false negative'. Even if the patient is classified as NSTEMI of 'very high-risk', receives timely intervention and has the diagnosis of ACO confirmed, something

that occurred in only 6% of very high-risk patients in a recent registry, their diagnosis will still be 'NSTEMI'. The patient's condition will not be retrospectively called 'STEMI' as a surrogate for ACO.<sup>4</sup> This creates the 'no false negative paradox'.

This problem creates another bias: 'feedback sanction'.<sup>5</sup> Because of incorporation bias, false negative cases are so difficult to perceive that medical practitioners often receive no feedback on their failure to diagnose ACO because the practitioner did not fail to diagnose 'STEMI'; instead, they correctly diagnosed NSTEMI but this is a diagnosis which does not reflect ACO. Without such feedback, such as they might get on a prolonged door-to-balloon time for STEMI, the opportunity to learn is missing, and thus, the problem does not exist from their perspective. If all their diagnoses of NSTEMI are considered to be correct, the STEMI-NSTEMI paradigm does not need to be questioned. For example, discharge diagnoses change to highlight false positive STEMI but not false negative STEMI and this fact prevents providers from learning about missed occlusions.<sup>6</sup>

## THE AVAILABILITY CASCADE AND COGNITIVE COMFORT

A realistic demonstration of this scenario can be observed through a hypothetical yet commonly encountered clinical case in emergency rooms, coronary units and cardiology wards: A patient presents with symptomatic, ongoing ACO (so, the pathophysiological process was present) and therefore needs urgent reperfusion but without STE, consequently a false negative. The diagnosis established by the team was NSTEMI and he underwent catheterisation outside the optimal door-to-balloon time even though the hospital was equipped for primary angioplasty. ACO was eventually identified during the hospitalisation and angioplasty and stent placement were performed. The patient then proceeded to the coronary unit where he spent several more days hospitalised. The patient's ejection fraction is low, the troponin is very high (a reasonable measure of infarct size) and, perhaps, heart failure occurs. While it must be noted that these outcomes are not exclusive to ACO and can also arise from incomplete occlusion and other acute coronary syndromes, the key point here is the misclassification of ACO. When time comes for discharge, the discharge summary is 'NSTEMI'. It is very likely that the team will never ask this question: 'But the coronary artery

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was occluded in this patient, and there was substantial loss of myocardium. Should not the diagnosis be something other than NSTEMI? Could we not have salvaged more myocardium if we had recognised ACO sooner and provided timely reperfusion?' Because there was no STE, the diagnosis ('NSTEMI') is deemed correct. This patient with a large infarct due to complete ACO received the same diagnosis as a patient with pathophysiological process which is similar but on the exact opposite end of the severity spectrum.

From the perspective of the attending team at that hospital, everything appears to be satisfactory; that is, there is no mandated feedback provided regarding this diagnostic oversight due to the incorporation bias deep-seated in the universal definition of myocardial infarction. Consequently, in many similar cases, no lessons

are drawn. Over years of encountering these scenarios, healthcare professionals have grown resistant to reconsidering the nomenclature, anchored by their comfort with the prevalent knowledge and the extensive body of literature supporting the STEMI-NSTEMI paradigm, a bias named 'availability cascade'.<sup>7</sup> This adherence to the familiar, together with resistance to critical reassessment and innovation is a state of mind named 'cognitive comfort' and posits itself as a formidable obstacle to the development of a classification system that better reflects the underlying pathophysiology in MI (figure 1).

### CONCLUSION

The discourse surrounding the diagnosis of an ACO causing MI reveals a complex interplay of biases that challenge the accuracy and efficacy of current medical

practice. 'Incorporation bias' leads to the 'no false negative paradox' where the absence of test criteria leads to a failure to recognise the disease in false negatives because the test defines or contains parts of the definition of the disease. Consequently, the disease does not exist, by definition, when the test is negative. This problem is further exacerbated by the 'feedback sanction bias'. In the STEMI-NSTEMI paradigm, healthcare professionals are deprived of crucial feedback on diagnostic errors which hinders learning and improvement. These biases collectively contribute to a systemic problem in medical diagnostics in which adherence to nomenclatures and paradigms prevails over evolving evidence and understanding despite clear indications of pathophysiological errors.

## THE NO FALSE NEGATIVE PARADOX

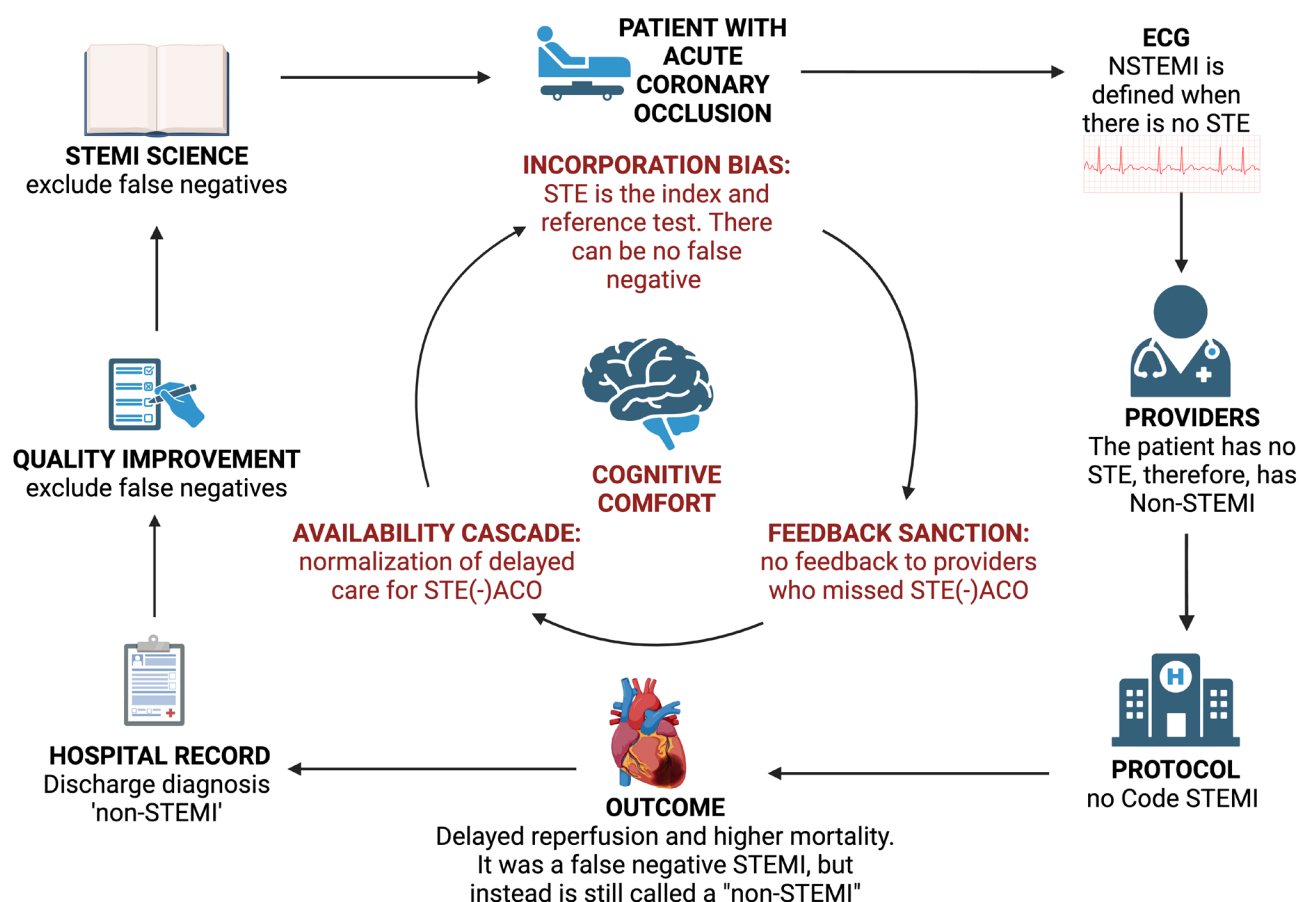


**Figure 1** The no false negative paradox and associated cognitive biases. Caption: Cognitive map of the current STEMI/NSTEMI paradigm. The outer circle shows how reliance on STEMI criteria leads to delayed reperfusion for false negatives and how these missed occlusions are excluded from the medical record, quality improvement and STEMI research. This is reinforced by a series of cognitive biases which maintain cognitive comfort in the STEMI paradigm and resistance to change. ACO, acute coronary occlusion; STE, ST-segment elevation; STEMI, ST-segment elevation myocardial infarction.

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**Contributors** JNdA, HPM, JTTM and SWS were involved in the study design, data acquisition and interpretation of results. All authors contributed equally to the planning, conduct and reporting of the work described in the article. They were also involved in drafting and critically reviewing the manuscript. All authors approved the final version. JNdA, HPM, JTTM and SWS share the responsibility as guarantors of this manuscript.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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**To cite** de Alencar JN, Meyers HP, McLaren JTT, *et al.* *Heart* Epub ahead of print: [please include Day Month Year]. doi:10.1136/heartjnl-2024-324512

*Heart* 2024;0:1–3.  
doi:10.1136/heartjnl-2024-324512

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